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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/013,077	01/26/1998	JEFFREY L. NAUSS		2904

7590 06/20/2003

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EXAMINER
CELSA, BENNETT M

ART UNIT	PAPER NUMBER
1639	37

DATE MAILED: 06/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

file copy

Office Action Summary

Application No.	Applicant(s)
09/013,077	Naus et al.
Examiner	**Art Unit**
Bennett Celsa	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 21, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *15, 18, 21, 22, 25, 26, 48, and 49* is/are pending in the application.

4a) Of the above, claim(s) *18* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *15, 21, 22, 25, 26, 48, and 49* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

Applicant's amendment dated 4/21/03 in paper no. 36 is hereby acknowledged.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

Claims 15, 18, 21-22, 25, 26, 48 and 49 are pending.

Claim 18 is withdrawn from consideration.

Claims 15, 21-22, 25, 26, 48 and 49 are under consideration only to the extent that they read on the elected invention (e.g. compositions of peptides comprising seq. Id. 3).

Election/Restriction

2. Applicant's election without traverse of Group I (claims 15, 21-23, 25, 26, 48 and 49 drawn to compositions comprising a 16 amino acid peptide of seq. Id 3) in Paper No.33 is again acknowledged.

3. Claim 18 and the part of claims 15, 21-23, 25, 26, 48 and 49 which are directed to fragments of seq. Id 3 or other sequence id's other seq. Id 3 (e.g. Groups II-XVI) are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

4. This application contains nonelected claims 15, 21-22, 25, 26, 48 and 49 . A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Objection(s) and/or Rejection (s)

Applicant's amendment has overcome the objection of claims 21, 22 and 25 under 37 CFR 1.75(c), as being of improper dependent form.

In light of applicant's amendment and arguments relating thereto the enablement rejection of claims 15, 21-23, 25, 26, 48 and 49 is hereby withdrawn.

Applicant's amendment and arguments relating thereto have overcome the rejection of claims 15, 21-23, 25, 26, 48 and 49 under 35 U.S.C. 112, second paragraph,

Outstanding Objection (s) and/or Rejection (s)

5. Claims 15, 21-22, 25, 26, 48 and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (NEW MATTER REJECTION). .

A. To the extent that Applicant's amendment (e.g. paper no. 13: dated 6/28/00) of claim 15 can be interpreted to encompass obtaining "minimized peptides" beyond those peptides having (e.g. comprising) seq. Id. 3; the increased scope constitutes new matter. Amending the claim to remove terminology such as "is minimized" and "minimized peptide" (e.g. to recite "... a peptide in which the peptide binds to a class ... etc) will overcome this rejection.

With regard to item A. above, it is noted that the specification fails to provide direct support or examples of peptides which are representative of the additional scope; nor has applicant indicated where such specification support exists. Applicant must cancel the new matter in response to this rejection.

Discussion

Applicant's amendment and argument directed to the above rejection was found persuasive with regard to item B (e.g. by canceling claim 23) but nonpersuasive with regard to item a. It is noted that the above rejection was modified in response to applicant's amendment.

Applicant argues that "The Examiner objects to the term "minimized as new matter" a term which is argued by applicant to bes supported by the specification pages 3-4.

Applicant has mischaracterized the above rejection. The rejection states that the specification and original claims provide support for a single species of peptide (e.g. seq. Id 3) within the generic of species that comprise seq. Id 3 which are optionally capable of being **"minimized"** (e.g. conformationally change or otherwise "alter the peptide(s) to accommodate the receptor: see specification pages 3-4) to bind Class II MHC receptor DR1 and inhibit the binding of HA residues 306-318. There is no direct specification or original claim support for the newly claimed generic of peptides nor is a single peptide of seq. Id 3 which is "minimized" to bind to a Class II MHC receptor DR1 and inhibit the binding of HA residues 306-318 representative of the ability of the generic of peptides which **comprise** seq. Id 3 to be capable of

being "minimized" (w/n the broad scope of this term)and bind Class II MHC receptor DR1 and inhibit the binding of HA residues 306-318.

Applicant argues that original claims 5 and 15 which together recite any minimized peptide which binds a Class II MHC receptor DR1 and inhibits the binding of HA (306-318) provide the requisite support.

This argument is not persuasive since it fails to provide support for the newly claimed generic of peptides ***comprising*** seq. Id 3 which may be (e.g. "wherein when said peptide ....") "minimized (e.g. "altered") to bind receptor and tested for immunogenicity. Claims 5 and 15 do not refer to seq. Id 3 or a generic comprising seq. Id 3 which may be "minimized" to bind "Class II MHC receptor DR1 and inhibit the binding of HA residues 306-318 to which there is no specification support.

Accordingly, the above rejection, as modified, is hereby maintained.

6. Claims 15, 21-22 and 48 are rejected under 35 U.S.C. 102(a) as being anticipated by Nauss et al. Journal of Immunology Vol. 150/No. 8 part II, No. 221 (April 15, 1993) in view of specification pages 12-13 to demonstrate inherency.

The Nauss et al. article teaches a synthetic antigenic T-cell epitope of the pilus protein of enterotoxigenic E. Coli (ETEC) representing residues 63-78 of the ETEC CS3 pilus protein (CS3 63-78) which inhibits the binding of radio-labeled synthetic peptide or residues 307-319 of the influenza hemagglutinin protein (HA 307-319) to purified DR1 Class II MHC in a direct binding

assay. The T-cell epitope for CS3 pilus protein subunit 63-78 corresponds to Ser-Lys-Asn-Gly-Thr-Val-Thr-Trp-Ala-His-Glu-Thr-Asn-Asn-Ser-Ala (Seq. Id No: 3) of the CS3 protein, as presently claimed thus rendering the Nauss et al. compositions anticipatory regarding the immunogenic compositions presently claimed. See present specification. Intended use (e.g. minimization etc. and/or use as a vaccine against various microbes/neoplasms in claims 21-22) in compound/composition claims lack patentable weight. Additionally, to the extent that the reference teaching of the reference peptide being "antigenic" fails to suggest immunogenicity; such characteristics would be deemed to be inherent to the reference composition which contain an antigenic peptide and compositions thereof within the scope of the presently claimed invention.

7. Claims 15, 21-22, 25, 26, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nauss et al. Journal of Immunology Vol. 150/No. 8 part II, No. 221 (April 15, 1993) and the specification pages 12-13 to demonstrate inherency in view of Reid et al. U.S. Pat. No. 5,417,986 (5/95: filed 4/92 or earlier) .

The Nauss et al. article teaches a synthetic antigenic T-cell epitope of the pilus protein of enterotoxigenic E. Coli (ETEC) representing residues 63-78 of the ETEC CS3 pilus protein (CS3 63-78) which inhibits the binding of radio-labeled synthetic peptide or residues 307-319 of the influenza hemagglutinin protein (HA 307-319) to purified DR1 Class II MHC in a direct binding assay. The T-cell epitope for CS3 pilus protein subunit 63-78 corresponds to Ser-Lys-Asn-Gly-

Thr-Val-Thr-Trp-Ala-His-Glu-Thr-Asn-Asn-Ser-Ala (Seq. Id No: 3) of the CS3 protein, as presently claimed thus rendering the Nauss et al. compositions anticipatory regarding the immunogenic compositions presently claimed. See present specification. Intended use (e.g. as a vaccine against various microbes/neoplasms in claims 21-22) in compound/composition claims lack patentable weight. Additionally, to the extent that the reference teaching of the reference peptide being "antigenic" fails to suggest immunogenicity; such characteristics would be deemed to be inherent to the reference composition which contain an antigenic peptide within the scope of the presently claimed invention.

The Nauss et al. reference differs from the presently claimed invention in failing to teach incorporating its "antigenic" pilus peptide into a pharmaceutical composition comprising a carrier [e.g. biodegradable-biocompatible microspheres (DL-lactide-co-glycolactide)].

Reid et al. teach oral/parenteral/intestinal vaccine compositions and their use against diseases caused by enteropathogenic organisms (e.g. E. Coli) using antigens encapsulated within biodegradable-biocompatible microspheres (DL-lactide-co-glycolactide) . See e.g. abstract; col. 3-4; See Examples and Patent claims. The use of the microsphere carrier prevents the degrading or complexing with secretory IgA in the intestinal lumen of uncomplexed protein antigens. E.g. See Reid et al. Col. 1, especially lines 35-60.

Accordingly, the Reid et al. patent provides motivation (e.g. prevent degradation and unintended immune complexing) to one of ordinary skill in the art to make pharmaceutical compositions comprising the Nauss et al. "antigenic" pilus peptide in microsphere carriers in

order to formulate pharmaceutical compositions capable of use as vaccine compositions against pathogenic microorganisms (e.g. including E. Coli.).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to incorporate the Nauss "antigenic" pilus peptide into a pharmaceutical composition comprising a carrier [e.g. biodegradable-biocompatible microspheres (DL-lactide-co-glycolactide)] as taught by Reid et al. in order to formulate pharmaceutical compositions intended for use as vaccines against pathogenic microorganisms such as E.Col. .

Discussion

Applicant's arguments directed to the above anticipation and obviousness rejections over the Nauss reference taken separately or in combination with other references were considered but deemed nonpersuasive for the following reasons. It is noted that the above rejection was modified in response to applicant's amendment.

Applicant argues that the present application claims priority of serial no. 08/064,559 (filed May 21, 1993) which is asserted to anti-date the Nauss et al. Article.

This argument is not persuasive for the following reasons.

First, the publication date of the article (by an entity different from the present inventors) appears to antedate applicant's assertion of 35 USC 120 priority of 08/064,559 (filed May 21, 1993). Secondly, to the extent the presently claimed invention contains new matter (e.g. see new matter rejection) priority under 35 USC 120 for any prior application must be denied.

Accordingly, the above anticipation rejection is hereby maintained.

8. Claims 15, 21-22, 25, 26, 48 and 49 are rejected under 35 U.S.C. 102(e) as being anticipated by Reid et al. U.S. Pat. No. 5,417,986 (5/95: filed 4/92 or earlier) in view of specification pages 12-13 to demonstrate inherency

Reid et al. teach oral/parenteral/intestinal vaccine compositions and their use against diseases caused by enteropathogenic organisms (e.g. E. Coli) using antigens encapsulated within biodegradable-biocompatible microspheres (DL-lactide-co-glycolactide) . See e.g. abstract; col. 3-4; See Examples and Patent claims. The Reid et al. patent further teaches that the CS3 protein is known; and the use of a CFA/II microsphere vaccine and other immunogenic compositions suggests the presence and use of CS3 protein in such compositions. See e.g. Examples; col 37-38 (especially lines 31-54). The reference teaching of CS3 protein and/or vaccine compositions comprising the CS3 protein anticipate the presently claimed compositions since the CS3 protein necessarily comprises presently claimed Seq. Id 3 since the T-cell epitope for CS3 pilus protein subunit 63-78 corresponds to Ser-Lys-Asn-Gly-Thr-Val-Thr-Trp-Ala-His-Glu-Thr-Asn-Asn-Ser-Ala (Seq. Id No: 3) of the CS3 protein. See present specification. It is noted that intended use (e.g.minimization etc. and/or use as a vaccine against various microbes/neoplasms in claims 21-22) in compound/composition claims lack patentable weight

Discussion

Applicant's arguments directed to the above anticipation rejection were considered but deemed nonpersuasive for the following reasons. It is noted that the above rejection was modified in response to applicant's amendment

Applicant argues that the present application is directed to encapsulation of CS3 peptides. This is not persuasive since only dependent claim 49 is directed to encapsulation and in any event the Reid reference teaches encapsulating microspheres within the scope of the present application.

Applicant argues that claim 15 requires a "peptide, wherein when said peptide is minimized, the minimized peptide binds to a Class II MHC receptor DR1" and the Reid reference fails to disclose that the entire protein binds Class II MHC receptor DR1" and "one would not necessarily conclude that a protein would bind to the model because a peptide fragment binds to the model".

These arguments are not persuasive for several reasons.

First, as written, the claim 15 limitation regarding minimization, as recited above (e.g. " wherein *when said peptide is minimized*, the minimized peptide binds to a Class II MHC receptor DR1") appears to be an optional limitation and thus not required..

Secondly the above recited limitation is clearly intended use which is not afforded patentable weight.

Thirdly, the the reference immunogenic peptide clearly meets the presently claimed structural requirement of "having" (or comprising) seq. Id No. 3 and thus is clearly within the scope of the presently claimed invention. Assuming arguendo that there is any patentable weight whatsoever afforded to the intended use limitation, the burden is on applicant to demonstrate that the reference peptide cannot be "minimized" (e.g. conformationally change or otherwise "alter

the peptide(s) to accommodate the receptor: see specification pages 3-4) such that it binds to a Class II MHC receptor DR1 and inhibits the binding of HA residues 306-318. In this respect the metes and bounds of peptide alterations to accomplish "minimization" would appear to encompass peptide fragmentation (if necessary to achieve minimization) of the reference peptide. In this regard, it is noted that the Examiner lacks the necessary facilities to perform modeling, binding and other assays necessary to evaluate mimimization, binding inhibition or immunogenicity.

Accordingly, the above rejection, as modified, is hereby maintained.

9. Claims 15, 21-22, 25, 26, 48 and 49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,309,669 (10/01).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent claims teach pharmaceutical compositions comprising encapsulated (e.g. biodegradable poly lactide/glycolide) "biologically active agents" including immunogenic (e.g. vaccine) peptides (e.g. antibacterial/antiviral). See e.g. patent claims 1-9. The claims encompass preferred "biologically active agents" which include the CS3 peptide 63-78 corresponding to present sequence id 3 . See col. 32 (especially item "112"); col. 33 (especially item "117"); col. 34 (especially item 133) the selection of which would have been prima facie obvious to one of ordinary skill in the art.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang (art unit 1639), can be reached at (703)306-3217.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1639)
June 18, 2003

BENNETT CELSA
PRIMARY EXAMINER